

AMENDMENTS TO THE CLAIMS

The following listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of claims:**1-11 (canceled).****12 (currently amended).** A compound selected from:

~~2-(5-[3-[3-(4-Fluoro-phenyl)-prop-1-ynyl] phenyl]-tetrazol-2-ylmethyl)-oxazole-4-carboxylic acid;~~

~~4-(5-[3-[3-(4-Fluoro-phenyl)-prop-1-ynyl] phenyl]-tetrazol-2-ylmethyl)-benzoic acid;~~

~~4-(5-[5-[3-(4-Methoxy-phenyl)-prop-1-ynyl]-pyridin-3-yl]-tetrazol-2-ylmethyl)-benzoic acid;~~

~~[4-(5-[3-[3-(4-Fluoro-phenyl)-prop-1-ynyl] phenyl]-tetrazol-2-ylmethyl)-phenyl] acetic acid;~~

~~4-(5-[3-[3-(4-Fluoro-phenyl)-prop-1-ynyl] phenyl]-[1,3,4]thiadiazol-2-ylmethyl)-benzoic acid;~~

~~4-[5-[2-(4-Fluoro-benzylcarbamoyl)-pyridin-4-yl]-tetrazol-2-ylmethyl]-benzoic acid; and~~

~~4-(5-[3-[3-(4-Fluoro-phenyl)-prop-1-ynyl] phenyl]-tetrazol-2-ylmethyl)-cyclohexanecarboxylic acid;~~

~~1-[4-(5-[3-[3-(4-Fluoro-phenyl)-prop-1-ynyl] phenyl]-tetrazol-2-ylmethyl)-phenyl] cyclopropanecarboxylic acid;~~

~~3-(5-[3-[3-(4-Fluoro-phenyl)-prop-1-ynyl] phenyl]-tetrazol-2-ylmethyl)-benzoic acid; and~~

~~4-[5-[2-(4-Fluoro-benzylcarbamoyl)-6-methyl-pyridin-4-yl]-tetrazol-2-ylmethyl]-benzoic acid; or~~

a pharmaceutically acceptable salt thereof.

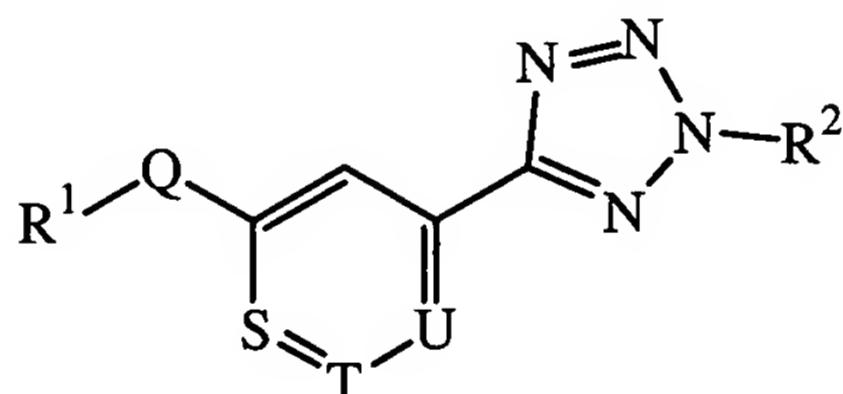
13 (canceled).

14 (currently amended). The A pharmaceutical composition, comprising a compound according to Claim 12, or a pharmaceutically acceptable salt thereof, admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

15 (canceled).

16 (previously presented). A method for treating osteoarthritis or rheumatoid arthritis, comprising administering to a patient suffering from osteoarthritis or rheumatoid arthritis a nontoxic effective amount of a compound according to Claim 12, or a pharmaceutically acceptable salt thereof.

17 (currently amended). A compound of Formula II



II

or a pharmaceutically acceptable salt thereof,

wherein:

R¹ and R² independently are selected from:

H;

C₁-C₆ alkyl;

Substituted C₁-C₆ alkyl;

C₂-C₆ alkenyl;

Substituted C₂-C₆ alkenyl;

C₂-C₆ alkynyl;

Substituted C₂-C₆ alkynyl;

C₃-C₆ cycloalkyl;
Substituted C₃-C₆ cycloalkyl;
C₃-C₆ cycloalkyl-(C₁-C₆ alkylenyl);
Substituted C₃-C₆ cycloalkyl-(C₁-C₆ alkylenyl);
3- to 6-membered heterocycloalkyl;
Substituted 3- to 6-membered heterocycloalkyl;
3- to 6-membered heterocycloalkyl-(C₁-C₆ alkylenyl);
Substituted 3- to 6-membered heterocycloalkyl-(C₁-C₆ alkylenyl);
Phenyl-(C₁-C₆ alkylenyl);
Substituted phenyl-(C₁-C₆ alkylenyl);
Naphthyl-(C₁-C₆ alkylenyl);
Substituted naphthyl-(C₁-C₆ alkylenyl);
5-, 6-, 9-, and 10-membered heteroaryl-(C₁-C₆ alkylenyl);
Substituted 5-, 6-, 9-, and 10-membered heteroaryl-(C₁-C₆ alkylenyl);
Phenyl;
Substituted phenyl;
Naphthyl;
Substituted naphthyl;
5-, 6-, 9-, and 10-membered heteroaryl;
Substituted 5-, 6-, 9-, and 10-membered heteroaryl;
R³O-(C₁-C₆ alkylenyl); and
Substituted R³O-(C₁-C₆ alkylenyl);
~~Phenyl~~;
~~Substituted phenyl~~;
~~Naphthyl~~;
~~Substituted naphthyl~~;
5- or 6-membered heteroaryl;
Substituted 5- or 6-membered heteroaryl;
8- to 10-membered heterobiaryl;
Substituted 8- to 10-membered heterobiaryl;

Phenyl-O-(C₁-C₈ alkylenyl);
Substituted phenyl-O-(C₁-C₈ alkylenyl);
Phenyl-S-(C₁-C₈ alkylenyl);
Substituted phenyl-S-(C₁-C₈ alkylenyl);
Phenyl-S(O)-(C₁-C₈ alkylenyl);
Substituted phenyl-S(O)-(C₁-C₈ alkylenyl);
Phenyl-S(O)₂-(C₁-C₈ alkylenyl); and
Substituted phenyl-S(O)₂-(C₁-C₈ alkylenyl);

wherein R¹ and R² are not both selected from:

H;
C₁-C₆ alkyl;
C₂-C₆ alkenyl;
C₂-C₆ alkynyl; and
C₃-C₆ cycloalkyl;

wherein at least one of R¹ and R² is independently selected from:

C₃-C₆ cycloalkyl-(C₁-C₆ alkylenyl); and
Substituted C₃-C₆ cycloalkyl-(C₁-C₆ alkylenyl);

Each R³ independently is selected from:

H;
C₁-C₆ alkyl;
Substituted C₁-C₆ alkyl;
C₃-C₆ cycloalkyl;
Substituted C₃-C₆ cycloalkyl;
Phenyl-(C₁-C₆ alkylenyl);
Substituted phenyl-(C₁-C₆ alkylenyl);
Naphthyl-(C₁-C₆ alkylenyl);
Substituted naphthyl-(C₁-C₆ alkylenyl);
5-, 6-, 9-, and 10-membered heteroaryl-(C₁-C₆ alkylenyl);
Substituted 5-, 6-, 9-, and 10-membered heteroaryl-(C₁-C₆ alkylenyl);

Phenyl;

Substituted phenyl;

Naphthyl;

Substituted naphthyl;

5-, 6-, 9-, and 10-membered heteroaryl;

Substituted 5-, 6-, 9-, and 10-membered heteroaryl;

~~S, T, and U each are C-R⁴; or~~

One of S, T, and U is N and the other two of S, T, and U are C-R⁴; or

~~Two of S, T, and U are N and the other one of S, T, and U is C-R⁴;~~

Each R⁴ independently is selected from:

H;

F;

CH₃;

CF₃;

C(O)H;

CN;

HO;

CH₃O;

C(F)H₂O;

C(H)F₂O; and

CF₃O;

Q is N(R⁶)C(O);

R⁶ is H, C₁-C₆ alkyl, C₃-C₆ cycloalkyl; 3- to 6-membered heterocycloalkyl;

phenyl; benzyl; or 5- or 6-membered heteroaryl;

Each "substituted" group contains from 1 to 4 substituents, each independently on a carbon or nitrogen atom, independently selected from:

C₁-C₆ alkyl;

C₂-C₆ alkenyl;

C₂-C₆ alkynyl;

C₃-C₆ cycloalkyl;

C₃-C₆ cycloalkylmethyl;
Phenyl;
Phenylmethyl;
3- to 6-membered heterocycloalkyl;
3- to 6-membered heterocycloalkylmethyl;
cyano;
CF₃;
(C₁-C₆ alkyl)-OC(O);
HOCH₂;
(C₁-C₆ alkyl)-OCH₂;
H₂NCH₂;
(C₁-C₆ alkyl)-N(H)CH₂;
(C₁-C₆ alkyl)₂-NCH₂;
N(H)₂C(O);
(C₁-C₆ alkyl)-N(H)C(O);
(C₁-C₆ alkyl)₂-NC(O);
N(H)₂C(O)N(H);
(C₁-C₆ alkyl)-N(H)C(O)N(H);
N(H)₂C(O)N(C₁-C₆ alkyl);
(C₁-C₆ alkyl)-N(H)C(O)N(C₁-C₆ alkyl);
(C₁-C₆ alkyl)₂-NC(O)N(H);
(C₁-C₆ alkyl)₂-NC(O)N(C₁-C₆ alkyl);
N(H)₂C(O)O;
(C₁-C₆ alkyl)-N(H)C(O)O;
(C₁-C₆ alkyl)₂-NC(O)O;
HO;
(C₁-C₆ alkyl)-O;
CF₃O;
CF₂(H)O;
CF(H)₂O;

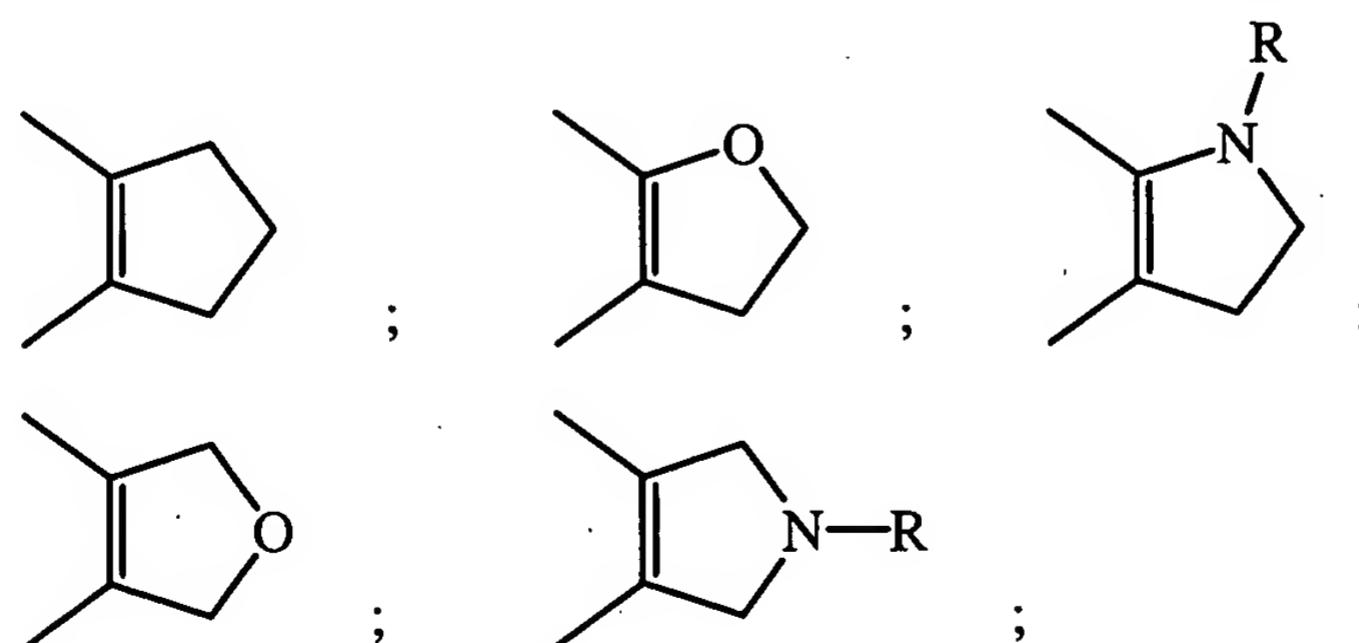
$\text{H}_2\text{N};$
 $(\text{C}_1\text{-C}_6 \text{ alkyl})\text{-N}(\text{H});$
 $(\text{C}_1\text{-C}_6 \text{ alkyl})_2\text{-N};$
 $\text{O}_2\text{N};$
 $(\text{C}_1\text{-C}_6 \text{ alkyl})\text{-S};$
 $(\text{C}_1\text{-C}_6 \text{ alkyl})\text{-S(O);}$
 $(\text{C}_1\text{-C}_6 \text{ alkyl})\text{-S(O)}_2;$
 $(\text{C}_1\text{-C}_6 \text{ alkyl})_2\text{-NS(O)}_2;$
 $(\text{C}_1\text{-C}_6 \text{ alkyl})\text{-S(O)}_2\text{-N}(\text{H})\text{-C(O)}\text{-}(\text{C}_1\text{-C}_8 \text{ alkylene})_m;$ and
 $(\text{C}_1\text{-C}_6 \text{ alkyl})\text{-C(O)-N(H)-S(O)}_2\text{-}(\text{C}_1\text{-C}_8 \text{ alkylene})_m;$

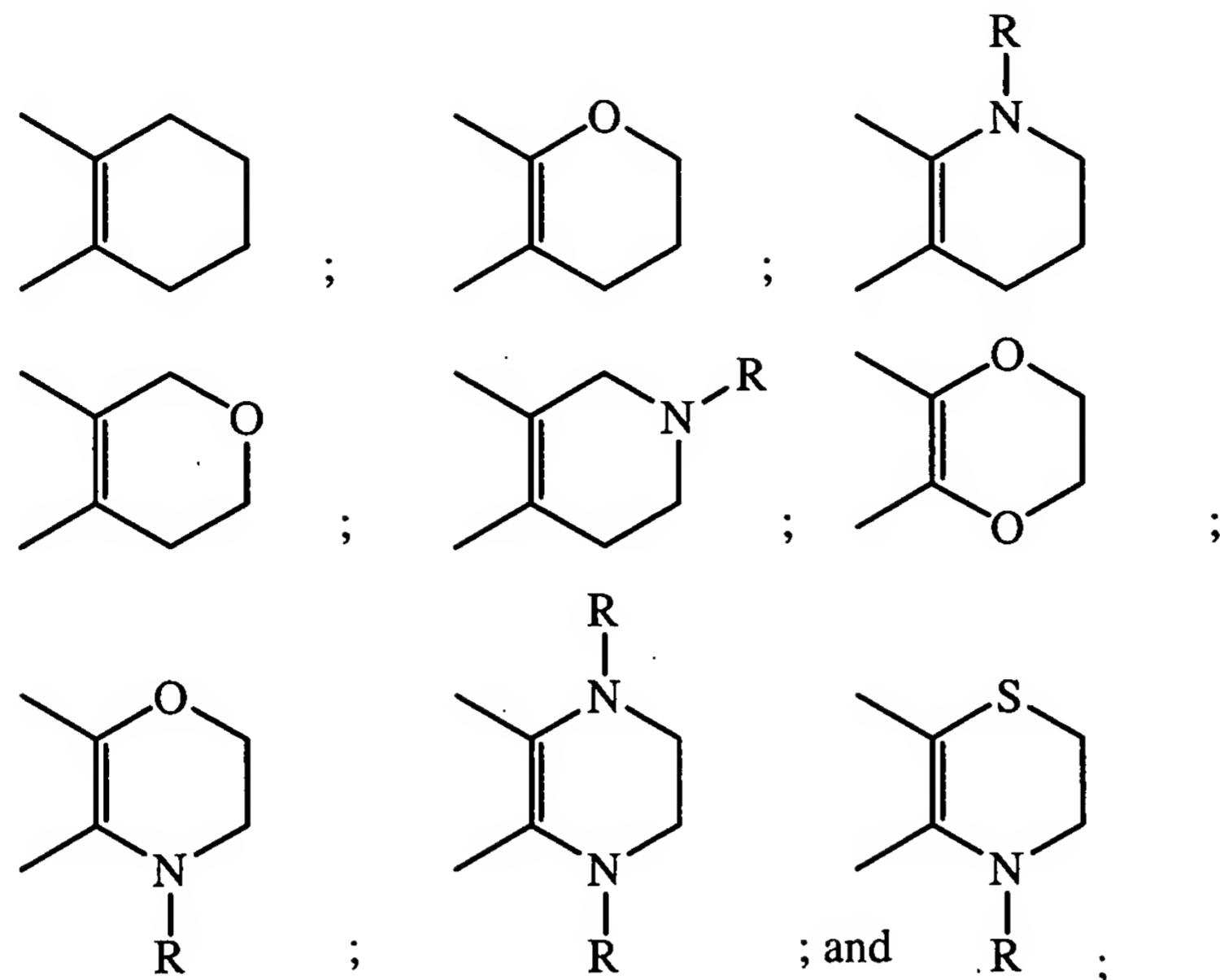
wherein each substituent on a carbon atom may further be independently selected from:

Halo;
 $\text{HO}_2\text{C};$ and
 $\text{OCH}_2\text{O},$ wherein each O is bonded to adjacent carbon atoms to form a 5-membered ring;

wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group $\text{C=O};$

wherein two adjacent, substantially sp^2 carbon atoms may be taken together with a diradical substituent to form a cyclic diradical selected from:





R is H or C₁-C₆ alkyl;

m is an integer of 0 or 1;

wherein each 5-membered heteroarylenyl independently is a 5-membered ring containing carbon atoms and from 1 to 4 heteroatoms selected from 1 O, 1 S, 1 NH, 1 N(C₁-C₆ alkyl), and 4 N, wherein the O and S atoms are not both present, and wherein the heteroarylenyl may optionally be unsubstituted or substituted with 1 substituent selected from fluoro, methyl, hydroxy, trifluoromethyl, cyano, and acetyl;

wherein each heterocycloalkyl is a ring that contains carbon atoms and 1 or 2 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 S(O)₂, 1 N, 2 N(H), and 2 N(C₁-C₆ alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond;

wherein each 5-membered heteroaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C₁-C₆ alkyl), and 4 N, and each 6-membered heteroaryl contains carbon atoms

and 1 or 2 heteroatoms independently selected from N, N(H), and N(C₁-C₆ alkyl), and 5- and 6-membered heteroaryl are monocyclic rings; and 9- and 10-membered heteroaryl are 6,5-fused and 6,6-fused bicyclic rings, respectively, wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O and S atoms both are present, the O and S atoms are not bonded to each other;
wherein with any (C₁-C₆ alkyl)₂-N group, the C₁-C₆ alkyl groups may be optionally taken together with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocycloalkyl; and
wherein each group and each substituent recited above is independently selected.

18 (previously presented). The compound according to claim 17, wherein Q is N(H)C(O).

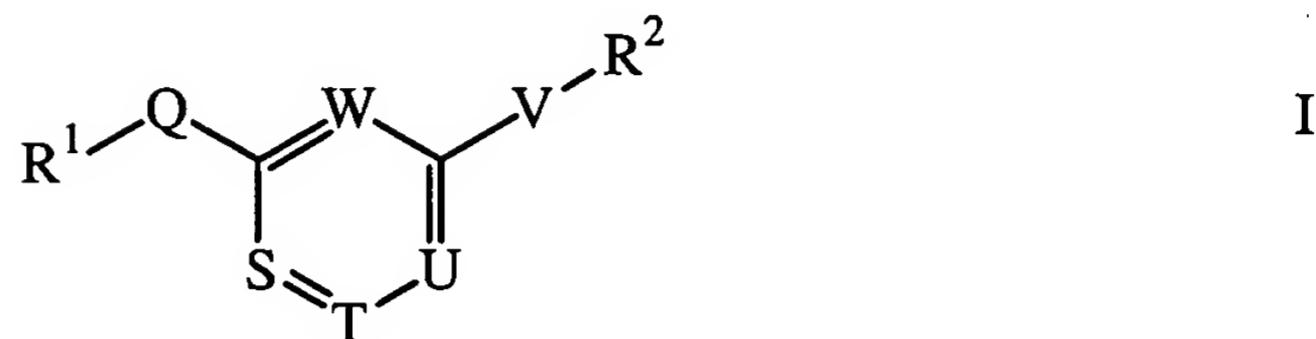
19 (previously presented). The compound according to claim 18, wherein each C₁-C₆ alkylene is CH₂.

20 (previously presented). The compound according to claim 19, wherein at least one substituent is selected from the group consisting of:

CO₂H;
CO₂CH₃;
CH₃O;
F;
Cl;
CN;
CF₃;
CH₃S(O)₂;
CH₃; or

wherein at least two substituents are Cl and F, 2 F, or OCH₂O, wherein each O is bonded to adjacent carbon atoms to form a 5-membered ring.

21 (currently amended). A compound of Formula I



or a pharmaceutically acceptable salt thereof,
wherein:

R¹ and R² independently are selected from:

- H;
- C₁-C₆ alkyl;
- Substituted C₁-C₆ alkyl;
- C₂-C₆ alkenyl;
- Substituted C₂-C₆ alkenyl;
- C₂-C₆ alkynyl;
- Substituted C₂-C₆ alkynyl;
- C₃-C₆ cycloalkyl;
- Substituted C₃-C₆ cycloalkyl;
- C₃-C₆ cycloalkyl-(C₁-C₆ alkylenyl);
- Substituted C₃-C₆ cycloalkyl-(C₁-C₆ alkylenyl);
- 3- to 6-membered heterocycloalkyl;
- Substituted 3- to 6-membered heterocycloalkyl;
- 3- to 6-membered heterocycloalkyl-(C₁-C₆ alkylenyl);
- Substituted 3- to 6-membered heterocycloalkyl-(C₁-C₆ alkylenyl);
- Phenyl-(C₁-C₆ alkylenyl);
- Substituted phenyl-(C₁-C₆ alkylenyl);
- Naphthyl-(C₁-C₆ alkylenyl);
- Substituted naphthyl-(C₁-C₆ alkylenyl);
- 5-, 6-, 9-, and 10-membered heteroaryl-(C₁-C₆ alkylenyl);

Substituted 5-, 6-, 9-, and 10-membered heteroaryl-(C₁-C₆ alkylenyl);
Phenyl;
Substituted phenyl;
Naphthyl;
Substituted naphthyl;
5-, 6-, 9-, and 10-membered heteroaryl;
Substituted 5-, 6-, 9-, and 10-membered heteroaryl;
R³O-(C₁-C₆ alkylenyl);
Substituted R³O-(C₁-C₆ alkylenyl);
Phenyl;
~~Substituted phenyl~~;
~~Naphthyl~~;
~~Substituted naphthyl~~;
5- or 6-membered heteroaryl;
Substituted 5- or 6-membered heteroaryl;
8- to 10-membered heterobiaryl;
Substituted 8- to 10-membered heterobiaryl;
Phenyl-O-(C₁-C₈ alkylenyl);
Substituted phenyl-O-(C₁-C₈ alkylenyl);
Phenyl-S-(C₁-C₈ alkylenyl);
Substituted phenyl-S-(C₁-C₈ alkylenyl);
Phenyl-S(O)-(C₁-C₈ alkylenyl);
Substituted phenyl-S(O)-(C₁-C₈ alkylenyl);
Phenyl-S(O)₂-(C₁-C₈ alkylenyl); and
Substituted phenyl-S(O)₂-(C₁-C₈ alkylenyl);

wherein R¹ and R² are not both selected from:

H;
C₁-C₆ alkyl;
C₂-C₆ alkenyl;

C₂-C₆ alkynyl; and

C₃-C₆ cycloalkyl;

Each R³ independently is selected from:

H;

C₁-C₆ alkyl;

Substituted C₁-C₆ alkyl;

C₃-C₆ cycloalkyl;

Substituted C₃-C₆ cycloalkyl;

Phenyl-(C₁-C₆ alkylene);

Substituted phenyl-(C₁-C₆ alkylene);

Naphthyl-(C₁-C₆ alkylene);

Substituted naphthyl-(C₁-C₆ alkylene);

5-, 6-, 9-, and 10-membered heteroaryl-(C₁-C₆ alkylene);

Substituted 5-, 6-, 9-, and 10-membered heteroaryl-(C₁-C₆ alkylene);

Phenyl;

Substituted phenyl;

Naphthyl;

Substituted naphthyl;

5-, 6-, 9-, and 10-membered heteroaryl;

Substituted 5-, 6-, 9-, and 10-membered heteroaryl;

S is N and T, U, and W each are C-R⁴; or

~~S is N, one of T, U, and W are N, and the other two of T, U, and W are C-R⁴; or~~

~~T is C-R⁴ and S, U, and W are each N; or~~

~~U is C-R⁴ and S, T, and W are each N;~~

Each R⁴ independently is selected from:

H;

F;

CH₃;

CF₃;

C(O)H;

CN;
HO;
CH₃O;
C(F)H₂O;
C(H)F₂O; and
CF₃O;

V is a 5-membered heteroarylenyl;

Q is N(H)C(O);

Each "substituted" group contains from 1 to 4 substituents, each independently on a carbon or nitrogen atom, independently selected from:

C₁-C₆ alkyl;
C₂-C₆ alkenyl;
C₂-C₆ alkynyl;
C₃-C₆ cycloalkyl;
C₃-C₆ cycloalkylmethyl;
Phenyl;
Phenylmethyl;
3- to 6-membered heterocycloalkyl;
3- to 6-membered heterocycloalkylmethyl;
cyano;
CF₃;
(C₁-C₆ alkyl)-OC(O);
HOCH₂;
(C₁-C₆ alkyl)-OCH₂;
H₂NCH₂;
(C₁-C₆ alkyl)-N(H)CH₂;
(C₁-C₆ alkyl)₂-NCH₂;
N(H)₂C(O);
(C₁-C₆ alkyl)-N(H)C(O);
(C₁-C₆ alkyl)₂-NC(O);

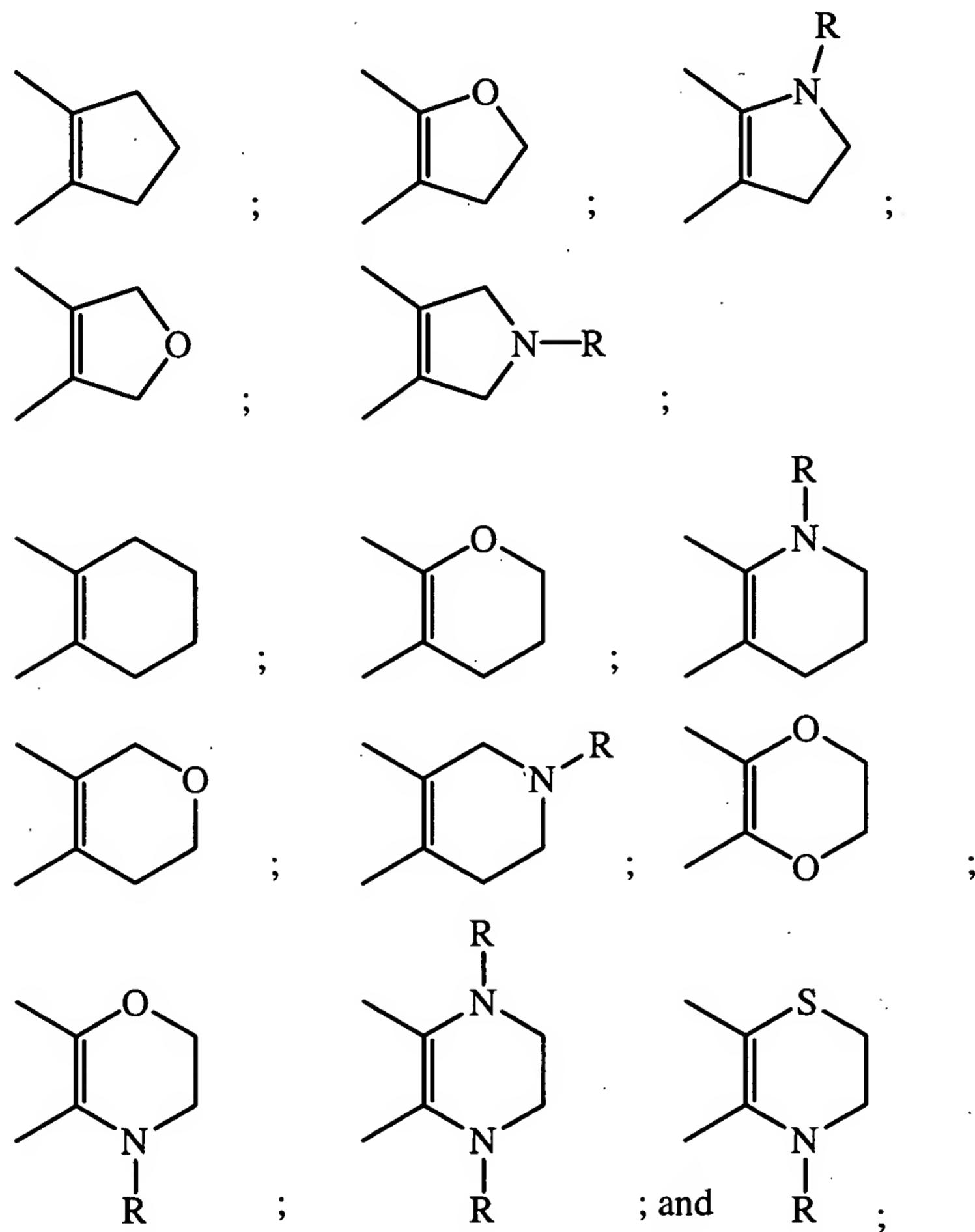
N(H)₂C(O)N(H);
(C₁-C₆ alkyl)-N(H)C(O)N(H);
N(H)₂C(O)N(C₁-C₆ alkyl);
(C₁-C₆ alkyl)-N(H)C(O)N(C₁-C₆ alkyl);
(C₁-C₆ alkyl)₂-NC(O)N(H);
(C₁-C₆ alkyl)₂-NC(O)N(C₁-C₆ alkyl);
N(H)₂C(O)O;
(C₁-C₆ alkyl)-N(H)C(O)O;
(C₁-C₆ alkyl)₂-NC(O)O;
HO;
(C₁-C₆ alkyl)-O;
CF₃O;
CF₂(H)O;
CF(H)₂O;
H₂N;
(C₁-C₆ alkyl)-N(H);
(C₁-C₆ alkyl)₂-N;
O₂N;
(C₁-C₆ alkyl)-S;
(C₁-C₆ alkyl)-S(O);
(C₁-C₆ alkyl)-S(O)₂;
(C₁-C₆ alkyl)₂-NS(O)₂;
(C₁-C₆ alkyl)-S(O)₂-N(H)-C(O)-(C₁-C₈ alkylene)_m; and
(C₁-C₆ alkyl)-C(O)-N(H)-S(O)₂-(C₁-C₈ alkylene)_m;

wherein each substituent on a carbon atom may further be independently selected from:

Halo;
HO₂C; and
OCH₂O, wherein each O is bonded to adjacent carbon atoms to form a 5-membered ring;

wherein 2 substituents may be taken together with a carbon atom to which they are both bonded to form the group C=O;

wherein two adjacent, substantially sp^2 carbon atoms may be taken together with a diradical substituent to form a cyclic diradical selected from:



R is H or C₁-C₆ alkyl;

m is an integer of 0 or 1;

wherein each 5-membered heteroarylenyl independently is a 5-membered ring

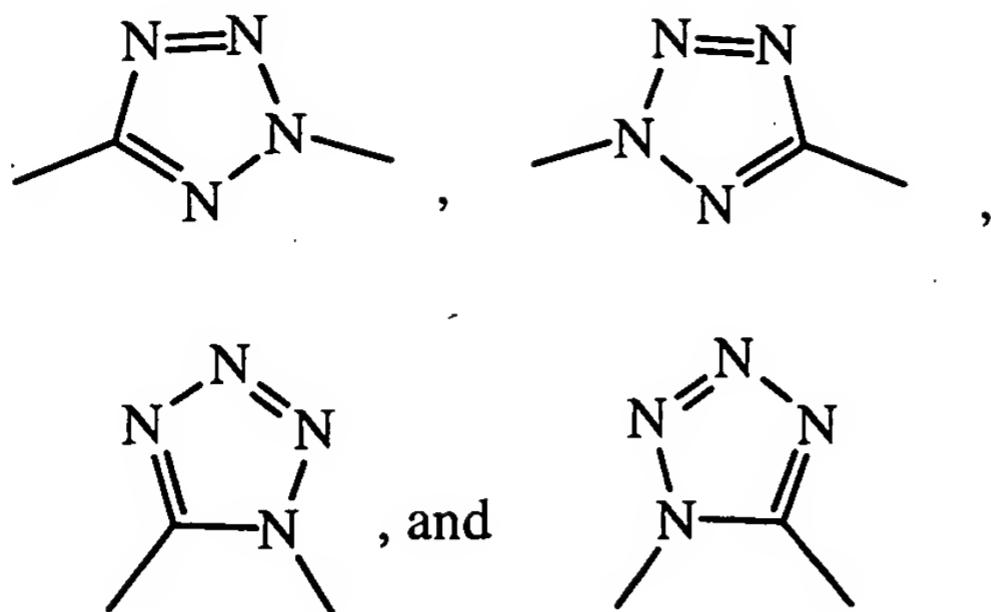
containing carbon atoms and from 1 to 4 heteroatoms selected from 1 O, 1

S, 1 NH, 1 N(C₁-C₆ alkyl), and 4 N, wherein the O and S atoms are not

both present, and wherein the heteroarylenyl may optionally be

unsubstituted or substituted with 1 substituent selected from fluoro, methyl, hydroxy, trifluoromethyl, cyano, and acetyl; wherein each heterocycloalkyl is a ring that contains carbon atoms and 1 or 2 heteroatoms independently selected from 2 O, 1 S, 1 S(O), 1 S(O)₂, 1 N, 2 N(H), and 2 N(C₁-C₆ alkyl), and wherein when two O atoms or one O atom and one S atom are present, the two O atoms or one O atom and one S atom are not bonded to each other, and wherein the ring is saturated or optionally contains one carbon-carbon or carbon-nitrogen double bond; wherein each 5-membered heteroaryl contains carbon atoms and from 1 to 4 heteroatoms independently selected from 1 O, 1 S, 1 N(H), 1 N(C₁-C₆ alkyl), and 4 N, and each 6-membered heteroaryl contains carbon atoms and 1 or 2 heteroatoms independently selected from N, N(H), and N(C₁-C₆ alkyl), and 5- and 6-membered heteroaryl are monocyclic rings; and 9- and 10-membered heteroaryl are 6,5-fused and 6,6-fused bicyclic rings, respectively, wherein at least 1 of the 2 fused rings of a bicyclic ring is aromatic, and wherein when the O and S atoms both are present, the O and S atoms are not bonded to each other; wherein with any (C₁-C₆ alkyl)₂-N group, the C₁-C₆ alkyl groups may be optionally taken together with the nitrogen atom to which they are attached to form a 5- or 6-membered heterocycloalkyl; and wherein each group and each substituent recited above is independently selected.

22 (previously presented). The compound according to claim 21, wherein V is selected from the group consisting of:



23 (previously presented). The compound according to claim 22, wherein at least one of R¹ and R² is independently selected from:

C₃-C₆ cycloalkyl-(C₁-C₆ alkylene); and

Substituted C₃-C₆ cycloalkyl-(C₁-C₆ alkylene).

24 (previously presented). The compound according to claim 23, wherein each C₁-C₆ alkylene is CH₂.

25 (previously presented). The compound according to claim 24, wherein at least one substituent is selected from the group consisting of:

CO₂H;

CO₂CH₃;

CH₃O;

F;

Cl;

CN;

CF₃;

CH₃S(O)₂;

CH₃; or

wherein at least two substituents are Cl and F, 2 F, or OCH₂O, wherein each O is bonded to adjacent carbon atoms to form a 5-membered ring.

26 (previously presented). A pharmaceutical composition comprising a compound according to any one of claims 17 and 21, or a pharmaceutically acceptable salt thereof; admixed with a pharmaceutically acceptable carrier, excipient, or diluent.

27 (previously presented). A method for treating osteoarthritis, comprising administering to a patient suffering from osteoarthritis a nontoxic effective amount of a compound according to one of claims 17 and 21, or a pharmaceutically acceptable salt thereof.

28 (previously presented). A method for treating rheumatoid arthritis, comprising administering to a patient suffering from rheumatoid arthritis a nontoxic effective amount of a compound according to one of claims 17 and 21, or a pharmaceutically acceptable salt thereof.